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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/032,229	12/20/2001	George Jackowski	2132.113	3487

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EXAMINER	
TURNER, SHARON L	

ART UNIT	PAPER NUMBER
1649	

DATE MAILED: 01/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/032,229	JACKOWSKI ET AL.	
	Examiner	Art Unit	
	Sharon L. Turner	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 December 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) *5-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-12* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12-20-01* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *9-29-03* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *IDS 4-24-02* .

DETAILED ACTION

1. The petition decision of 11-14-05 for revival is noted. The amendment filed 6-27-05 has been entered and fully considered.

2. Claims 1-12 are pending.

Election/Restrictions

3. Applicant's election without traverse of Group II, claims 1-4 in the reply filed on 6-27-05 is acknowledged.

4. Claims 5-12 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 6-27-05.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for detection of thrombospondin, does not reasonably provide enablement for diagnosis of dementia via detection of a marker indicative of thrombospondin or of thrombosponding in body fluid from mammalian samples. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification is insufficient to enable one skilled in the art to practice the

invention as broadly claimed without undue experimentation. The factors relevant to this discussion include the quantity of experimentation necessary, the lack of working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims.

Applicants claims are directed to diagnosis of dementia via detection of a marker indicative of thrombospondin or of thrombospondin in body fluid from mammals.

The specification does not enable the broad scope of the claims because the specification fails to delineate those markers that are suitably indicative of thrombospondin besides detection of thrombospondin itself. Further the specification fails to delineate any suitably correlative marker, thrombospondin or otherwise that is indicative of the diagnosis of dementia.

The art recognizes that even today definitive diagnosis of dementia as a condition in and of itself is confounding because of mental decline that may be linked to a plethora of diseases and/or condiditons. For example, dementia is associatively developed in patients with the clinically distinct pathologies of Down's syndrome, Parkinson's, Huntington's, vascular disease or stroke as well as Alzheimer's disease. Cognitive decline is also recognized among normal aged patients. The closest diagnostic measure is that as delineated in DSM criteria, but it is not definitively associated as a singular disease or disease state, see in particular de Mendonca et al., J Mol Neurosci. 2004;23(1-2):143-8, Mild cognitive impairment: focus on diagnosis, Misciagna et al., Int J Neurosci. 2005 Dec;115(12):1657-67, Vascular dementia and Alzheimer's disease: the unsolved problem of clinical and neuropsychological

differential diagnosis, Kilada et al., Alzheimer Dis Assoc Disord. 2005 Jan-Mar;19(1):8-16, Brief screening tests for the diagnosis of dementia: comparison with the mini-mental state exam and Storey et al., Int Psychogeriatr. 2004 Mar;16(1):13-31, The Rowland Universal Dementia Assessment Scale (RUDAS): a multicultural cognitive assessment scale. Even so, the specification fails to distinguish correlation of any particular marker with any art accepted measure that is indicative and correlative to dementia diagnosis. Accordingly, no basis is provided that thrombospondin or thrombospondin markers are diagnostically indicative of any particular disease state or particular to dementia. While thrombospondin is recognized as being present in Alzheimer's plaque pathology and normal brain, see in particular Buee et al., American journal of pathology, (1992 Oct) 141 (4) 783-8, Immunohistochemical identification of thrombospondin in normal human brain and in Alzheimer's disease, such is not diagnostic to dementia. Moreover, thrombospondin is noted to be detected in biological mammalian fluids not associated with dementia conditions, see for example Clezardin et al., Journal of chromatography, (1984 Jul 27) 296 249-56, Isolation of thrombospondin released from thrombin-stimulated human platelets by fast protein liquid chromatography on an anion-exchange Mono-Q column and Lawler et al., Blood, (1986 Feb) 67 (2) 555-8, Thrombospondin in essèntial thrombocythemia. This raises the issue that detection of thrombospondin or thrombospondin markers in blood are not definitive of dementia and would provide reference or sample testing subject to false positive diagnosis.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such guidance, the

changes which can be made and still maintain activity/utility is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Int. 1986). Thus, the skilled artisan cannot readily make and use the claimed sequences without further undue experimentation.

7. Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification is on point to the protein thrombospondin, which is asserted as being diagnostic to dementia. However, the claims as written are directed to the term "a marker indicative of thrombospondin". However, the specification fails to delineate markers that are "indicative of thrombospondin." The specification provides the following definition with respect to "marker" at pp. 10-11, "As used herein the term "marker" "biochemical marker" or "marker protein" refers to any enzyme, protein, polypeptide, peptide, isomeric form thereof, immunologically detectable fragments thereof, or other molecule, whose presence, absence, or variance in fluids from so-called "normal" levels, are circulating body indicative of dementia. Most particularly, such markers may be illustrated as being released from the brain during the course of dementia related changes, e.g. AD pathogenesis. Such markers include, but are not limited any unique proteins or isoforms thereof are particularly associated with the

brain." Yet such does not describe any member protein that is suitably "indicative of thrombospondin" and diagnostic to dementia.

A genus claim may be supported by a representative number of species as set forth in Regents of the University of California v Eli Lilly & Co, 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). For example, a description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus.

The instant specification discloses, however, a single polypeptide thrombospondin that is asserted to be diagnostic to dementia but provides no evidence for such correlation or for the correlation of any particular marker indicative of thrombospondin that provides for diagnosis. Accordingly, the scope of the genus recitation lacks evidence of even a single species member. Given the unpredictability of diagnostic correlative comparisons, and the fact that the specification fails to provide objective evidence of any species of the claimed genus it cannot be established that a representative number of species have been disclosed to support the genus claim. No correlative structural or functional activity for the marker is set forth. Accordingly, the claims lack adequate written description support.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are directed to the term "a marker indicative of thrombospondin". However, the specification fails to delineate markers that are indicative of thrombospondin. The specification provides the following definition with respect to marker at pp. 10-11, "As used herein the term "marker" "biochemical marker" or "marker protein" refers to any enzyme, protein, polypeptide, peptide, isomeric form thereof, immunologically detectable fragments thereof, or other molecule, whose presence, absence, or variance in fluids from so-called "normal" levels, are circulating body indicative of dementia. Most particularly, such markers may be illustrated as being released from the brain during the course of dementia related changes, e.g. AD pathogenesis. Such markers include, but are not limited any unique proteins or isoforms thereof are particularly associated with the brain." However, such does not clarify whether any brain associated protein exhibiting such modulation is appropriate or whether particular ones are intended. Accordingly, the scope of the claim cannot be determined.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the

applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

11. Claims 1-4 are rejected under 35 U.S.C. 102(e) as being anticipated by Ni et al., US 6605592 or in the alternative Ni et al., US PGPub 20020068319. These references are cumulative and are therefore cited together with identical reasoning therefore.

Ni teaches the peptide of thrombospondin and variants that are used for detection of dementia based on expression on platelets and in brain, see in particular column 22-93 of the patent. In addition as noted in the PGPpub, the invention includes antibodies to the protein and methods of detection from mammalian samples. In particular the methods include A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising: (a) determining the presence or amount of expression of the polypeptide of claim 11 in a biological sample; and (b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or amount of expression of the polypeptide, see in particular claim 19. The following excerpts are particularly noted.

Summary of Invention Paragraph:[0033] Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include but are not limited to: neurodegenerative disorders; immune system dysfunction; immunosuppression; transplant rejection; graft versus host disease; inflammatory disorders; and autoimmune diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the brain, CNS, and immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., neural, immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Brief Summary Text (96):Thrombospondin-1 (TSP-1) is a 450 kDa, anti-angiogenic adhesive glycoprotein released from activated platelets and secreted by growing cells (reviewed in Adams, Int. J. Biochem. Cell Biol. 29:861-865 (1997)). TSP-1 is a homotrimer, with each subunit comprised of a 1152 amino acid residue polypeptide, post-translationally modified by N-linked glycosylation and beta-hydroxylation of asparagine residues.

Brief Summary Text (97):

TSP-1 protein and mRNA levels are regulated by a variety of factors. TSP-1 protein levels are down-regulated by IL-1 alpha and TNF alpha. TSP-1 mRNA and protein levels are up-regulated by polypeptide growth factors including PDGF, TGF-beta, and bFGF (Bornstein, FASEB J. 6:3290-3299 (1992)) and are also regulated by the level of expression of the p53 tumor suppressor gene product (Dameron et al., Science 265:1582-1584 (1994)). At least four other members of the thrombospondin family have been identified: TSP-2, TSP-3, TSP-4, and TSP-5 (also called COMP). There is a need in the art to identify other molecules involved in the regulation of angiogenesis.

Brief Summary Text (99):

FIGS. 5A-5E shows the regions of identity between the amino acid sequence of THRAP and the translation product of Thrombospondin-like protein

Brief Summary Text (148):

The ubiquitous tissue distribution, the homology to thrombospondin-related protein, and the presence of multiple TSP-1-like domains indicates that the THRAP polypeptide and/or fragments of the present invention possess anti-angiogenic activity and, therefore, can be used in the treatment, diagnosis, and/or prevention of solid tumors of many tissues including, but not limited to the prostate, lung, breast, ovarian, stomach, pancreas, larynx, esophagus, testes, liver, parotid, biliary tract, colon, rectum, cervix, uterus, endometrium, kidney, bladder, thyroid cancer. Additionally, the THRAP polypeptide and/or fragments of the present invention can be used in the treatment, diagnosis, and/or prevention of primary tumors and metastases; melanomas; glioblastoma; Kaposi's sarcoma; leiomyosarcoma; non-small cell lung cancer; colorectal cancer; advanced malignancies; and blood born tumors such as leukemias.

Brief Summary Text (151):

The tissue distribution in brain and homology to thrombospondin-related protein indicates that the THRAP polypeptide and/or fragments of the present invention are useful for the detection, treatment, and/or prevention of neurodegenerative disease states, behavioral disorders, or inflammatory conditions. Representative uses are described in the "Regeneration" and "Hyperproliferative Disorders" sections below, in Example 11, 15, and 18, and elsewhere herein. Briefly, the uses include, but are not limited to the detection, treatment, and/or prevention of Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, Tourette's Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, depression, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and perception. In addition, elevated expression of this gene product in regions of the brain indicates it may play a role in normal neural function. Potentially, THRAP polypeptide and/or fragments of the present invention may be involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival.

Brief Summary Text (152):

The tissue distribution in immune cells and tissues (e.g., macrophage, and lymph node) and homology to thrombospondin-related protein indicates that the THRAP polypeptide and/or fragments of the present invention are useful for the detection, treatment, and/or prevention of a variety of immune system disorders. Representative uses are described in the "Immune Activity" and "Infectious Disease" sections below, in Example 11, 13, 14, 16, 18, 19, 20, and 27, and elsewhere herein. Briefly, the expression of this THRAP polypeptide and/or fragments of the present invention indicates a role in regulating the proliferation; survival; differentiation; and/or activation of hematopoietic cell lineages, including blood stem cells. This gene product is involved in the regulation of cytokine production, antigen presentation, or other processes suggesting a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product is involved in immune functions. Therefore it is also useful as an agent for immunological disorders including arthritis, asthma,

immunodeficiency diseases such as AIDS, leukemia, rheumatoid arthritis, granulomatous disease, inflammatory bowel disease, sepsis, acne, neutropenia, neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, such as autoimmune infertility, lens tissue injury, demyelination, systemic lupus erythematosis, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, and scleroderma. Moreover, the protein may represent a secreted factor that influences the differentiation or behavior of other blood cells, or that recruits hematopoietic cells to sites of injury. Thus, this gene product is thought to be useful in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. The expression within fetal tissue and other cellular sources marked by proliferating cells and homology to thrombospondin-related proteins indicates this protein may play a role in the regulation of cellular division, and may show utility in the diagnosis, treatment, and/or prevention of developmental diseases and disorders, including cancer, and other proliferative conditions. Representative uses are described in the "Hyperproliferative Disorders" and "Regeneration" sections below and elsewhere herein. Briefly, developmental tissues rely on decisions involving cell differentiation and/or apoptosis in pattern formation. Dysregulation of apoptosis can result in inappropriate suppression of cell death, as occurs in the development of some cancers, or in failure to control the extent of cell death, as is believed to occur in acquired immunodeficiency and certain neurodegenerative disorders, such as spinal muscular atrophy (SMA). Because of potential roles in proliferation and differentiation, this gene product may have applications in the adult for tissue regeneration and the treatment of cancers. It may also act as a morphogen to control cell and tissue type specification. Therefore, the polynucleotides and polypeptides of the present invention are useful in treating, detecting, and/or preventing said disorders and conditions, in addition to other types of degenerative conditions. Thus the THRAP polypeptide and/or fragments of the present invention may modulate apoptosis or tissue differentiation and would be useful in the detection, treatment, and/or prevention of degenerative or proliferative conditions and diseases. The THRAP polypeptide and/or fragments of the present invention are useful in modulating the immune response to aberrant polypeptides, as may exist in proliferating and cancerous cells and tissues. The THRAP polypeptide and/or fragments of the present invention can also be used to gain new insight into the regulation of cellular growth and proliferation.

Brief Summary Text (154):

Additionally, the expression of this gene product in synovium and homology to thrombospondin-related protein would suggest a role in the detection and treatment of disorders and conditions afflicting the skeletal system, in particular osteoporosis, bone cancer, connective tissue disorders (e.g. arthritis, trauma, tendonitis, chrondomalacia and inflammation). The THRAP polypeptide and/or fragments of the present invention are also useful in the diagnosis or treatment of various autoimmune disorders (i.e., rheumatoid arthritis, lupus, scleroderma, and dermatomyositis), dwarfism, spinal deformation, joint abnormalities, and chondrodysplasias (i.e. spondyloepiphyseal dysplasia congenita, familial osteoarthritis, Atelosteogenesis type II, metaphyseal chondrodysplasia type Schmid, etc.). Furthermore, the THRAP polypeptide and/or fragments of the present invention may also be used to determine biological activity, to raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that modulate their interactions, in addition to its use as a nutritional supplement. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Brief Summary Text (192):

Further, the expression of this gene in the nervous system of the human indicates that the polynucleotides and/or polypeptides corresponding to this gene, (and/or antibodies raised against those polypeptides) are useful in the detection, diagnosis and treatment of neurological conditions such as manic depression, Alzheimer's, Huntington's, and Parkinson's disease, Tourette's syndrome and other neurodegenerative diseases including but not limited to, demyelinating diseases, epilepsy, headache, migraine, CNS infections, neurological trauma and neural regrowth following trauma, CNS neoplasms, stroke and reperfusion injury following stroke. It may also be useful for the treatment and diagnosis of learning and cognitive diseases, depression, dementia, pyschosis, mania, bipolar syndromes,

schizophrenia and other psychiatric conditions. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival.

Accordingly, the reference teachings fairly anticipate a method for diagnosing dementia in a mammal via obtaining body fluid samples, detecting thrombosponding via antibodies and correlating the presence with dementia, including Alzheimer's.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ni et al., US 6605592 or in the alternative Ni et al., US PGPub 20020068319, further in view of Buee et al., (IDS) American journal of pathology, (1992 Oct) 141 (4) 783-8, Immunohistochemical identification of thrombospondin in normal human brain and in Alzheimer's disease, and WO98/07035 (IDS).

WO98/07035 teaches direct immunoassay amongst blood samples for the presence of thrombospondin, see in particular abstract, claims and throughout thereby teaching steps (a), (b) and (c).

The teachings of Ni et al are as noted above, similar to WO98/07035. Ni et al., note that dementia may be detected via such analysis for thrombospondin in blood. , but fail to tech the direct measurement or correlation of the presence of thrombospondin in blood with the occurrence of dementia.

Buee et al., notes that Thrombospondin is part of a family of adhesive glycoproteins and is involved in a number of physiologic processes such as angiogenesis and neurite outgrowth. Immunohistochemical localization of thrombospondin in normal human brains was investigated in the hippocampus and inferior temporal cortex. Two antibodies (one polyclonal and one monoclonal) against thrombospondin-labeled microvessels, glial cells, and a subpopulation of pyramidal neurons. The distribution of thrombospondin staining in patients with Alzheimer's disease was found to be comparable to control subjects. However, in patients with Alzheimer's disease a subset of pyramidal neurons that may be vulnerable in Alzheimer's disease exhibited decreased staining. This decrease in the intensity of labeling might constitute a marker for a neuronal population prone to early degeneration. In addition, thrombospondin staining was demonstrated in senile plaques in Alzheimer's disease. These results suggest that thrombospondin may be involved in the process of neuronal degeneration and senile plaque formation. Accordingly, Buee evidences the correlation of the presence of thrombospondin with the occurrence of dementia, even though the correlation was not in blood fluid, this is not a limitation of the claim. In short, thrombospondin detection in blood was known in addition to its presence in brains of dementia mammals, particularly within Alzheimer's patients.

Accordingly, the cumulative reference teachings motivate the artisan to diagnose dementia via detection of the correlation of thrombospondin with the occurrence of dementia and motivates the artisan to detect thrombospondin or thrombospondin variants via immunoassay from blood in correlation with its presence in brain pathology

associated with Alzheimer's Disease and dementia patients, thereby diagnosing dementia. Accordingly, the cumulative references render the claimed invention obvious to the artisan and establish an expectation of success as Buee evidences that the dementia patients are in fact correlated with the presence or detection of thrombospondin in blood via immunoassay.

Status of Claims

14. No claims are allowed.

Conclusion

15. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon L. Turner, Ph.D. whose telephone number is (571) 272-0894. The examiner can normally be reached on Monday-Thursday from 7:00 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached at (571) 272-0867.

Sharon L. Turner, Ph.D.
December 7, 2005

SHARON TURNER, PH.D.
PRIMARY EXAMINER
12-7-05